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# Response to 'Overexpression of complement-component genes in Han:SPRD rats a model of polycystic kidney disease'

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**We appreciate the letter submitted by Dr Burtey and co-workers in response to our recent report 'Overexpression of innate immune response genes in a model of recessive polycystic kidney disease'.[1] As noted in their letter,[2] these investigators observed that, similar to our observations in the *cpk* mouse model, genes encoding multiple innate immune factors, including complement system components, were overexpressed in Han:SPRD-*Cy* rat kidneys. Furthermore, in reviewing the table in their letter, we note additional gene expression similarities between these two models. For example, in *cpk* kidneys, we also observed increased expression of *Adamts1*, *Ctsd*, *Ctsk*, *Hmox1*, *Lyz* (under alias *Lzp-s*), *Mmp14*, and *Vim*. In addition, among the genes overexpressed in Han:SPRD-*Cy* kidneys, we have also observed increased expression of *F3*, *Lgals3*, *Mal*, and *Runx1* in *cpk* kidneys (data not shown in our original report). These significant parallels in gene expression profiles indicate that similar immune response pathways are activated in kidneys from two phenotypically distinct rodent models, suggesting that this perturbation may be a common signature of polycystic kidney disease.**

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# Need for a more realistic cut-off GFR value to define chronic renal failure

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**To the Editor:** We read with interest the article titled 'Age- and gender-specific reference values of estimated GFR in Caucasians: the Nijmegen Biomedical Study.' by Wetzels *et al.*,[1] and the commentary by Poggio *et al.*[2] titled 'Can we do better than a single estimated GFR threshold when screening for chronic kidney disease?' published in the September 2007 issue. We have performed a similar work in Indian population where we have measured glomerular filtration rate (GFR) in 610 healthy adults and demonstrated a mean GFR of 81.4 ml $min^{-1}$ compared with 83–85 ml $min^{-1}$ reported by Wetzels *et al.*[1,3]

The definition of decreased GFR relies on an understanding of the 'normal' GFR range. The Kidney Disease Outcome Quality Initiative guideline accepts normal GFR as 120 ml $min^{-1}$ and a 50% reduction in GFR ($<60$ ml $min^{-1}$) constitutes chronic renal failure (CRF).[4] It is universally accepted that GFR declines relentlessly with age; however, Kidney Disease Outcome Quality Initiative guideline assumes that GFR is stable between 18 and 70 years. This assumption allows a single cut-off GFR value for CRF. However, as has been demonstrated by Wetzels *et al.*, a 60 ml $min^{-1}$ cut-off tends to over-diagnose CRF. This problem gets accentuated in India, where normal GFR is itself lower by 25−30%. GFR of a 20-year-old Indian ranges from 89 to 109 ml $min^{-1}$ and a 50% reduction from normal translates into 45 ml $min^{-1}$. We agree with Wetzels *et al.* that GFR of 60 ml $min^{-1}$ cannot be used to define CRF. Consideration should be given to reduce the cut-off value for defining CRF, and we believe 45 ml $min^{-1}$ is more realistic in the Indian population.

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# Response to 'Need for a more realistic cutoff GFR value to define chronic renal failure'

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**We thank Drs Barai and Gambhir[1] for their thoughtful comments. Indeed, our paper intended to stimulate the discussion on 'normal' values. Obviously, reference values of glomerular filtration rate (GFR) may vary between populations. In the Indian population, GFR appears 20 ml min$^{-1}$ lower than in the European population.[2–4] It is important, however, to realize that differences in the methodology of GFR measurement may bias these results. In this respect, we wonder if Barai *et al.*[2] have used the correction factor of 1.15, which was proposed by Mulligan *et al.*[5] to improve the accuracy of GFR measurement using the Russel two point method. Thus, a GFR of 100 ml min$^{-1}$ should be corrected to 115 ml min$^{-1}$.**

**Most important is the definition of what is normal. As GFR decreases with age, it seems wise to use age-dependent reference values as 'normal' values. As such, the use of a fixed GFR cutoff point for defining chronic kidney disease is not logical. Still, the most important step is to define particular cutoff points that are independently associated with an increased risk of morbidity or mortality. Indeed, a recent study suggested that in elderly persons a lower GFR threshold should be used.[6] Certainly, more epidemiological data in different populations are needed. Meanwhile, we feel that in daily patient care, it is wise to compare the values of an individual patient with values obtained in age- and sex-matched controls.**

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